

CLAIMS

1. A recombinant gene medicine of adenovirus vector and p53 gene for treating proliferative disease, wherein it is constructed by adenovirus vector and human tumor suppressor p53 gene expression cassette, and its recombinant sequence is:
the right end of adenovirus 5 -
ATGTTTACCGCCACACTCGCAGGGTCTGCACCTGGTGCGGGTCTCATCGTAC
CTCAGCACCTTCCAGATC₇₀TCTGACATGCGATGTGCGACTCGACTGCTTCGCG
ATGTACGGGGCCAGATATACGCGTATCTGAGGGGACTAGGGTGTGTTTAGGGCG
10 AAAAGCGGGGCTTCGGTTGTACGCGGTTAGGAGTCCCCTCAGGATATAGTAG
TTTCGCTTTTGCATAGGGAGGGGGGAAATGTAGTCTTATGCAATACTCTTGTAG
TCTTGCAACATGGTAACGATGAGTTAGCAACATGCCTTACAAGGAGAGAAAAA
GCACCGTGATGCCGATTGGTGGAAAGTAAGGTGGTACGATCGTGCCTTATTA
GGAAGGCAACAGACGGGTCTGACATGGATTGGACGAACCACTGAATTCCGCA
15 TTGCAGAGATATTGTATTTAAGTGCCTAGCTCGATAACAATAAACGCCATTTGAC
CATTCACCACATTGGTGTGCACCTCCAAGCTTGGTACCGAGCTCGGATCCCG₅
₂₃CTAGAGCCACCGTCCAGGGAGCAGGTAGCTGCTGGGCTCCGGGGGACACTT
TGCGTTCGGGCTGGGAGCGTCTTTCCACGACGGTGACACGCTTCCCTGGATT
GGCAGCCAGACTGCTTTCCGGGTCACTGCC₆₅₅ATGGAGGAGCCGCGAGTCAGA
20 TCCTAGCGTCGAGCCCCCTCTGAGTCAGGAAACATTTTCAGACCTATGGAAAC
TACTTCCTGAAAACAACGTTCTGTCCCCCTTGCCGTCCCAAGCAATGGATGAT
TTGATGCTGTCCCCGGACGATATTGAACAATGGTTCACTGAAGACCCAGGTC
CAGATGAAGCTCCCAGAATGCCAGAGGCTGCTCCCCCGGTGGCCCCCTGCAC
CAGCAGCTCCTACACCGGCGGGCCCCCTGCACCAGCCCCCTCCTGGCCCCCTGT
25 CATCTTCTGTCCCTTCCCAGAAAACCTACCAGGGCAGCTACGGTTTCCGTCTG
GGCTTCTTGCAATTCTGGGACAGCCAAGTCTGTGACTTGCACGTACTCCCCCTG
CCCTCAACAAGATGTTTTGCCAACTGGCCAAGACCTGCCCTGTGCAGCTGTG
GGTTGATTCCACACCCCCGCCCGGCACCCGCGTCCGCGCCATGGCCATCTA
CAAGCAGTCACAGCACATGACGGAGGTTGTGAGGCGCTGCCCCCACCATGA
30 GCGCTGCTCAGATAGCGATGGTCTGGCCCCCTCCTCAGCATCTTATCCGAGTG
GAAGGAAATTTGCGTGTGGAGTATTTGGATGACAGAAACACTTTTCGACATAG
TGTGGTGGTGCCCTATGAGCCGCCTGAGGTTGGCTCTGACTGTACCACCATC
CACTACAACATCATGTGTAACAGTTCCTGCATGGGCGGCATGAACCGGAGGC
CCATCCTCACCATCATCACACTGGAAGACTCCAGTGGTAATCTACTGGGACG
35 GAACAGCTTTGAGGTGCGTGTTTGTGCCTGTCTGGGAGAGACCGGCGCACA
GAGGAAGAGAATCTCCGCAAGAAAGGGGAGCCTCACCACGAGCTGCCCCCA
GGGAGCACTAAGCGAGCACTGCCCAACAACACCAGCTCCTCTCCCCAGCCAA
AGAAGAAACCACTGGATGGAGAATATTTACCCCTTCAGATCCGTGGGCGTGA
GCGCTTCGAGATGTTCCGAGAGCTGAATGAGGCCTTGGAACCTCAAGGATGCC
40 CAGGCTGGGAAGGAGCCAGGGGGGAGCAGGGCTCACTCCAGCCACCTGAA
GTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAACTCATGTTCAAGACAG
AAGGGCCTGACTCAGACTGA₁₈₃₇CATTCTCCAATTCTTGTTCCTCCCACTGACAGC
CTCCACCCCCATCTCTCCCTCCCCTGCCATTTTGGGTTTTGGGTCTTTGAAC

CCTTGCTTGCAATAGGTGTGCGTCAGAAGCACCCAGGACTTCCATTTGCTTTG
 TCCCGGGGCTCCACTGAACAAGTTGGCCTGCACTGGTGTGTTTGTGTGGGGA
 GGAGGATGGGGAGTAGGACATACCAGCTTAGATTTTAAGGTTTTTACTGTGAG
 GGATGTTTGGGAGATGTAAGAAATGTTCTTGCAGTTAAGGGTTAGTTTACAAT
 5 CAGCCACATTCTAGGTAGGGGCCACTTCACCGTACTAACCAGGGAAGCTGTC
 CCTCACTGTTGAATTTTCTCTAACTTCAAGGCCCATATCTGTGAAATGCTGGAT
 TTGCCCTACCTCGGAATGCTGGCATTGTCACCTACCTCACAGAGTGCATTGTG
 AGGGTT₂₂₉₇AATGAAATAATGTACATCTGGCCTTGAAACCACCTTTTATTACATG
 GGGTCTAGCGGGATCCACTAGTAACGCCGCCAGTGTGCTGGAATTCTGCAGA
 10 TATCCATCACACTGGCGGCCGCTCGAGCATGCATCTAGAGCTCGCTGATCAG
 CCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGGCCCTCCCCCGTG
 CCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGA
 GGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG
 GTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCT
 15 GGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGC
 TCGAGGGGGATCCCCACGCTAGAGCT₂₇₃₃GACTATAATAATAAAACGCCAACT
 TTGACCCGGAACGCGGAAACACCTGAGAAAAACACCTGGGCGAGTCTCCAC
 GTAAACGGTCAAAGTCCCCGCGGCCCTAGACAAATATTA₂₈₄₈- the left end of
 adenovirus 5,

wherein:

- 1) the right end of adenovirus 5 and the left end of adenovirus 5 are described in the full sequence of adenovirus 5 (Genbank No: NC_001406)
- 2) 1-70: the right arm of adenovirus (the 70th base locates at adenovirus gene sequence 3328)
- 3) 71-523 : Rous Sarcoma Virus (RSV) LTR (promoter)
- 4) 524-655: 5' end non-translating region
- 5) 656-1837: p53 gene coding sequence
- 6) 1838-2733: 3' end non-translating region (poly Adenosine tail starting at 2298)
- 2734-2848: the left arm of adenovirus (base at 2734 is positioned at 452 of adenovirus 5 gene sequence).

2. The recombinant gene medicine according to Claim 1, wherein the gene expression cassette of the recombinant is a specific sequence composed of promoter-p53cDNA-poly adenosine.

3. The recombinant gene medicine according to claim 2, wherein the upstream of the gene expression cassette is any eukaryotic cell promoters, prokaryotic cell promoters or virus promoters, and the downstream is any of the eukaryotic gene poly adenosine residues (Poly A tail).

4. The recombinant gene medicine according to claim 1, wherein the recombinant gene medicine is obtained in prokaryotic cells by homologous recombination, including:

- 1) the recombinant pGT-2 is obtained by homologous recombination of adenovirus and plasmid pGT-1 (containing two inverted terminal repeats on both ends of adenovirus) in *E. coli*;
 - 2) the recombinant pGT-3 is obtained by homologous recombination of pGT-2 and artificial sequence "the right arm of adenovirus/ promoter-p53cDNA-poly A / the left arm of adenovirus " in *E. coli*;
 - 3) The recombinant p53 adenovirus is obtained by discarding the prokaryotic sequence using endonuclease *Pacl*.
5. The recombinant gene medicine according to claim 4, wherein the recombinant gene medicine is obtained in any prokaryotic cells by homologous recombination.
6. The recombinant gene medicine according to claim 1 is used to produce injection solution.
7. The recombinant gene medicine according to claim 6 is used to produce injection.